Paper No. 57

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte HANS-DETLEF DOPATKA

Appeal No. 2001-0544
Application No. 08/195,048

ON BRIEF

Before WINTERS, MILLS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 14, 15, 19-22, and 25, all of the claims remaining. Claim 25 is representative and reads as follows:

25. A method for determining the amount of an analyte in a biological sample, wherein said method is carried out by an instrument, comprising the steps of

a) contacting said biological sample with a solid-phase comprising a ligand specific for said analyte,

b) washing the solid-phase with a solution containing phenol or a phenol derivative carrying one or more substituents, wherein said substituents are C_1 to C_3-alkyl groups, chlorine or bromine,

c) removing the wash solution containing phenol or a phenol derivative,

d) detecting the amount of analyte bound to the solid-phase.

The examiner relies on the following references:

McClune et al. (McClune '999)	5,176,999	Jan. 05, 1993
McClune (McClune '983)	4,828,983	May 09, 1989
Katz et al. (Katz)	4,496,654	Jan. 29, 1985
Kricka et al. (Kricka)	4,598,044	Jul. 01, 1986
Wehner et al. (Wehner)	4,764,468	Aug. 16, 1988
Craig et al. (Craig)	4,810,630	Mar. 07, 1989

Claims 14, 15, 19-22, and 25 stand rejected under 35 U.S.C. § 103 as obvious in view of McClune '999, McClune '983, and Katz.[1]

Claims 14, 15, 19, 20, and 25 stand rejected under 35 U.S.C. § 103 as obvious in view of Kricka, Wehner, and Craig.

Claims 21 and 22 stand rejected under 35 U.S.C. § 103 as obvious in view of Kricka, Wehner, Craig, and McClune '999.

Claim 25 stands rejected under 35 U.S.C. § 112, first paragraph, for lack of adequate written description.

We reverse the obviousness rejections and affirm the written description rejection.

Background

The specification discloses "a washing solution, containing stabilizers for

[1] The statement of the rejection in the Examiner's Answer applied this rejection to claims "14-15, 18-22 and 25" (emphasis added). However, claim 18 had already been canceled. See Paper No. 29, filed January 9, 1997.

the labeling enzyme, for solid-phase immunometric assays, and . . . the use of this washing solution." Page 1. "Solid-phase immunometric assays, for example the enzyme-linked immunosorbent assay (ELISA), require one or more washing steps in the procedure. . . . [S]olid-phase immunometric assays can also be completed using instruments. This entails the washing steps being carried out by the instrument." Id.

Known washing solutions, however, have a disadvantage when the solid-phase immunometric assay is carried out using an instrument. See id., page 2: "When such instruments are used to complete the washing step, both the accuracy and the reproducibility of the measured signal reach an acceptable level only after some time, i.e. after some plates have been completed."

The specification discloses "a washing solution whose use in instruments makes possible correct completion of the ELISA even on immediate use of these devices." Id. The "addition of stabilizers achieves this object, irrespective of the buffer basis, the pH or other additives to the washing solution. Stabilizers within the meaning of this invention are substances which stabilize the labeling enzyme, such as, for example, tobramycin, phenol and phenol derivatives." Id. "Preferred stabilizers are phenols and phenol derivatives, in which case phenol can also carry one or more substituents which can be C_1-C_3-alkyl groups and chlorine and/or bromine atoms." Id., page 3.

Discussion

Claim 25 is the broadest claim on appeal and is directed to a method for detecting an analyte, comprising contacting a sample with a solid phase having

an analyte-specific ligand, "washing the solid phase with a solution containing phenol or a phenol derivative carrying one or more substituents, wherein said substituents are C_1 to C_3-alkyl groups, chlorine, or bromine," removing the wash solution, and detecting the bound analyte. The examiner rejected all of the claims as obvious and rejected claim 25 as lacking adequate descriptive support.

1. Obviousness

A. McClune '999, McClune '983, and Katz

The examiner rejected all of the claims as obvious in view of the disclosures of McClune '999, McClune '983, and Katz. The basis of the rejection is unclear from the Examiner's Answer. The Answer states that both McClune references "have been discussed supra," but the Examiner's Answer does not contain any previous discussion of either McClune reference. The examiner additionally cited McClune '983 as teaching a method for detecting human chronic gonadotropin (hCG), and stated that McClune '999 "differs from the instant invention in that they do not teach immobilization of the first antibody prior to contact with the sample (claim 14) and consequently that the complex of first antibody and analyte can be washed prior to contact with the second antibody (claim 20)." Examiner's Answer, page 6. The examiner cited Katz as teaching an immunological method of detecting hCG using a solid support having anti-hCG antibody attached to it via avidin/biotin coupling.

The examiner concluded that

> [i]t would have been obvious for one of ordinary skill in the art to immobilize the avidin-labeled first anti-hCG antibody of McClune ['999] prior to reaction with sample, since Katz et al. specifically

> teach a successful assay method which provides for the immobilization of an anti-hCG antibody prior to contact with the sample, and specifically teaches that such a method is highly sensitive and extremely simple to carry out. Although neither McClune ['999] or Katz et al. specifically teach washing of the antibody-analyte complex prior to incubation with enzyme-labeled antibody, such a step would have been obvious to one of ordinary skill in the art, since such modification of assay methods by inclusion of additional wash steps is well-known and conventional.

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant." In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). "The test of obviousness vel non is statutory. It requires that one compare the claim's 'subject matter as a whole' with the prior art 'to which said subject matter pertains." In re Ochiai, 71 F.3d 1565, 1569, 37 USPQ2d 1127, 1132 (Fed. Cir. 1995) (quoting 35 U.S.C. § 103).

In this case, the examiner has not carried the burden of showing prima facie obviousness of the claimed subject matter as a whole. Specifically, in the claimed method, after the solid support is contacted with a sample, it is washed with a solution containing phenol or a derivative of phenol substituted with a C_1 to C_3 alkyl group, chlorine, and/or bromine. The examiner has not explained why the cited references would have made it obvious to carry out such a washing step.

Every claim limitation is material and must be considered in the obviousness analysis. See In re Angstadt, 537 F.2d 498, 581, 190 USPQ 214,

217 (CCPA 1976) ("[W]e must give effect to all claim limitations.") (emphasis in original). See also General Foods Corp. v. Studiengesellschaft Kohle mbH, 972 F.2d 1272, 1275, 23 USPQ2d 1839, 1840 (Fed. Cir. 1992) ("[E]ach claim is an entity which must be considered as a whole.") (emphasis in original). The examiner has not shown that an immunoassay process including a step of washing with a solution containing phenol or one of the recited phenol derivatives would have been obvious in view of the prior art. Therefore, the examiner has not shown the prima facie obviousness of the claimed method as a whole. We reverse the rejection based on McClune '999, McClune '983, and Katz.

B. Kricka, Wehner, and Craig

The examiner rejected claims 14, 15, 19, 20, and 25 as obvious in view of the disclosures of Kricka, Wehner, and Craig. The examiner cited Kricka for "teach[ing] the use of phenolic compounds, including phenol derivatives having the instantly claimed substitutions . . . as enhancers of peroxidase activity in heterogeneous immunoassays." Examiner's Answer, page 7. The examiner conceded that Kricka does not "explicitly suggest the use of phenolic compounds in the wash solutions of the immunoassay." Id.

The examiner cited Wehner as "teach[ing] the stabilization of the activity of peroxidase in solution by the addition of phenol which optionally contains one or more substituents selected from lower alkyl radicals and chlorine and bromine atoms." Examiner's Answer, page 7. The examiner also noted that Wehner teaches that the phenol or phenol derivative can be added at any desired point in time to the enzyme or enzyme conjugate, in either solid or dissolved form, and

that it is preferably added to the enzyme in solution. Id., pages 7-8. Finally, the examiner cited Craig as teaching an assay buffer containing a polyoxyethylene ether detergent for immunoassays using peroxidase conjugates, and suggesting that a further advantage may be realized by including a polyoxyethylene ether detergent in wash solutions. Examiner's Answer, page 8.

The examiner concluded that

> [i]t would have been obvious to one of ordinary skill in the art to add phenolic compounds to the assay solutions, including the wash solutions, in the assays as taught by Kricka et al., since Wehner et al. specifically teach that the addition of such compounds in solution, to a solution of peroxidase or peroxidase conjugates, acts to stabilize the activity of peroxidase and that such compounds can be added at any desired point of time to the enzyme or enzyme conjugate and Craig et al. teaches that the addition of alternative formulations used for the improvement of the performance of peroxidase conjugates in assays into wash solution specifically, can produce further advantages in assays.

Id.

We agree with Appellant that the examiner has not made out a prima facie case of obviousness. It is true that both Kricka and Wehner teach advantages to using phenol or a phenol derivative in enzyme immunoassays using peroxidase as the enzymatic label. The advantages disclosed in the prior art, however, result from including both the phenol and the peroxidase in the same mixture. Kricka teaches that phenol enhances the activity of the peroxidase enzyme, while Wehner teaches that phenol stabilizes the peroxidase activity over time. See Kricka, column 2, lines 38-50 ("[T]here is provided an enhanced luminescent or luminometric assay, wherein the luminescent reaction is between a peroxidase enzyme, an oxidant, a chemiluminescent 2,3-dihydro-1,4-phthalazinedione and a

sensitivity enhancer of general formula I [i.e., phenol or substituted phenol]);" and Wehner, column 1, lines 49-55 ("[T]here is provided a process for stabilizing the activity of peroxidase in solution by the addition of a specific activity stabilizer, wherein, to the enzyme present in solid or dissolved form, there is added as activity stabilizer, phenol which optionally contains one or more substituents selected from lower alkyl radicals and chlorine or bromine atoms.").

Thus, in both Kricka and Wehner, the advantage disclosed to result from addition of phenol is gained through the addition of phenol to a peroxidase-containing solution. In the claimed method, by contrast, the solid phase of the immunoassay is washed with a phenol-containing solution. The wash solution is subsequently removed, and only then is the peroxidase- or other enzyme-containing solution added to detect the presence of bound analyte. See claim 25.

The examiner's references, and rejection based thereon, do not adequately address this difference between the prior art and the claimed process. Specifically, the examiner has not adequately explained why it would have been obvious to those skilled in the art to add phenol to a wash solution rather than to an enzyme-containing detection solution as disclosed in the prior art.

Craig does not provide the requisite motivation. Craig's disclosure is concerned only with the advantages to adding a polyoxyethylene ether detergent (e.g., Triton X-100®) to peroxidase-containing solutions. Craig discloses that such detergents improve the signal-to-noise ratio in immunoassays (column 2,

lines 36-42), and that the detergent can be added to, inter alia, wash solutions (column 3, lines 61-65). However, Craig does not teach or suggest that polyoxyethylene ether detergents and phenols have the same effect. Thus, the suggestion provided by Craig—to add a polyoxyethylene ether detergent to particular solutions—cannot be relied on to provide the required suggestion to add a phenol derivative to the same solutions.

The examiner has provided no other evidence or scientific reasoning to support combining the cited references. Since the record does not provide an adequate reason, suggestion, or motivation to combine the references, the rejection of claims 14, 15, 19, 20, and 25 under § 103 must be reversed.

The examiner also rejected claims 21 and 22 as obvious over Kricka, Wehner, and Craig, combined with McClune '999. Claims 21 and 22 depend on claim 14, and add the limitation that the labeling enzyme used in the claimed immunoassay is alkaline phosphatase (claim 21) or β-galactosidase (claim 22). The examiner cited McClune '999 as disclosing alkaline phosphatase and β-galactosidase as enzymes that could be substituted for the peroxidase used by Kricka and Wehner. Since the examiner cited McClune '999 only to meet the limitations of the dependent claims, McClune '999 does not remedy the deficiencies of Kricka, Wehner, and Craig, discussed above. The rejection of claims 21 and 22 is reversed as well.

2. Written description

The examiner rejected claim 25 under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description in the specification. The examiner

reasoned that the method defined in claim 25 is not limited to an enzyme immunoassay, while "[t]hroughout the specification it is clear that the only contemplated use of the claimed wash solution is in conjunction with an enzyme immunoassay for stabilization of the enzyme label. No where [sic] does the specification suggest or even hint that the claimed wash solution would be useful in any other kind of immunoassay." Examiner's Answer, page 5 (emphasis in original). Thus, the examiner concluded, the specification does not adequately support the method of claim 25, which encompasses "any and all types of immunoassays." Id.

We agree. The specification makes clear that it is the phenol-containing wash solution that distinguishes the claimed method from prior art assays. See page 1, line 22 ("Enzyme immunoassays as such are known."); page 1, lines 25-26 ("Solid phases for use in such enzyme immunoassays are likewise known."); page 1, lines 32-34 ("The known washing solutions . . . are composed, for example, of detergent-containing phosphate buffers."). See also page 2, lines 7-10 ("The present invention was therefore based on the object of finding a washing solution whose use in instruments makes possible correct completion of the ELISA even on immediate use of these devices."); page 2, lines 19-25 ("It has now been found, surprisingly, that the addition of stabilizers achieves this object. . . . Stabilizers within the meaning of this invention are substances which stabilize the labeling enzyme, such as, for example, tobramycin, phenol and phenol derivatives."); page 3, lines 20-23 ("Preferred stabilizers are phenols and

phenol derivatives, in which case phenol can also carry one or more substituents which can be C_1-C_3-alkyl groups and chlorine and/or bromine atoms.").

Thus, the specification makes clear that the defining characteristic of the claimed method is the inclusion of phenol (or a phenol derivative) in the wash solution, and that the phenol is added in order to "stabilize the labeling enzyme." It is therefore clear that the specification unambiguously limited the scope of its disclosure to wash solutions useful in enzyme immunoassays. That disclosure limits the permissible scope of later-added claims such as claim 25.

Appellant argues that the specification shows that he was in possession of the method of claim 25, citing page 1, lines 11-21 of the specification. Appeal Brief, pages 24-25. Appellant also argues that enzyme-linked immunosorbent assays (ELISAs) are only an example of solid-phase immunometric assays recited in claim 25. See the Reply Brief, pages 2-3.

These arguments are not persuasive. As discussed above, the specification makes clear that the phenol-containing wash solution is disclosed for use with enzyme immunoassays. Claim 25, by contrast, is not limited to enzyme immunoassays, or even, in fact, to immunoassays. By its terms, claim 25 encompasses any detection method in which an analyte is bound by a solid-phase "ligand," the solid phase is washed with a phenol-containing solution, and the analyte is then detected, by any means. The specification does not show that Appellant invented what is claimed by claim 25. Cf. Gentry Gallery, Inc. v. Berkline Corp., 134 F.3d 1473, 1479, 45 USPQ2d 1498, 1503 (Fed. Cir. 1998) ("To fulfill the written description requirement, the patent specification 'must

clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.'").

Gentry Gallery is instructive here. The invention in Gentry Gallery was a sofa having two reclining seats and a "console" between them that housed the controls for the seats. Id. at 1475, 45 USPQ2d at 1499. "[T]he original disclosure clearly identifie[d] the console as the only possible location for the controls. It provide[d] for only the most minor variation in the location of the controls. . . . No similar variation beyond the console [was] even suggested. . . . Thus, locating the controls anywhere but on the console [was] outside the stated purpose of the invention." Id. at 1479, 45 USPQ2d at 1503. In addition, the "broadest original claim was directed to a sofa comprising, inter alia, 'control means located upon the center console.'" Id. "[W]hen viewed in its entirety, the disclosure [was] limited to sofas in which the recliner control is located on the console." Id.

The inventor, however, later added claims that allowed the controls to be placed outside the console. The court found that these claims lacked an adequate written description. Id. at 1478, 45 USPQ2d at 1502. The specification made clear that the inventor "considered the location of the recliner controls on the console to be an essential element of his invention. Accordingly, his original disclosure serves to limit the permissible breadth of his later-drafted claims." Id. at 1479 45 USPQ2d at 1503. The caselaw makes clear that "claims may be no broader than the supporting disclosure, and therefore that a narrow disclosure will limit claim breadth." Id. Since the "disclosure unambiguously limited the

location of the controls to the console," id. at 1480, 45 USPQ2d at 1503-04, claims that lacked this limitation were held invalid for lack of descriptive support.

Gentry Gallery compels the conclusion in this case that the specification does not adequately describe the invention of claim 25. Just as the disclosure in Gentry Gallery unambiguously limited the location of the controls to the console, the disclosure in this application unambiguously limits the assay method to enzyme immunoassays. See pages 1-3, cited above. In addition, the claim is limited to methods "carried out by an instrument." The specification defines "instrument" as follows: "Instruments within the meaning of this invention are all instruments with whose aid washing steps in enzyme immunoassays can be carried out mechanically, irrespective of whether these instruments are able to carry out further steps in completing ELISA assays" (emphases added).

In Gentry Gallery, locating the controls outside the console was outside the stated purpose of the invention. Similarly here, the "invention was . . . based on the object of finding a washing solution whose use in instruments makes possible correct completion of the ELISA even on immediate use of these devices." Specification, page 2, lines 7-10 (emphasis added). The specification thus makes clear that assays other than enzyme immunoassays are outside the stated purpose of the invention. In Gentry Gallery, all the original claims required that the controls be located on the console. In this case, all the original claims were limited to enzyme immunoassays. See the originally filed claims (especially claims 1, 8, and 13).

Just as in Gentry Gallery, Appellant's original disclosure serves to limit the permissible breadth of the later-drafted claims. Claims may be no broader than the supporting disclosure, and therefore the narrow disclosure of the instant specification limits the allowable claim breadth. Instant claim 25, which encompasses assays other than the disclosed enzyme immunoassay, is not supported by an adequate written description in the originally filed specification. The rejection of claim 25 for inadequate written description is affirmed.

Summary

We reverse the rejections for obviousness because the cited references do not support a prima facie case under 35 U.S.C. § 103. However, we affirm the rejection of claim 25 as lacking adequate descriptive support because the specification does not provide adequate descriptive support for the scope of the claim. Thus, claims 14, 15, and 19-22 are not subject to any outstanding rejection.

AFFIRMED IN PART

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